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doi:10.1289/ehp.11451 (available at http://dx.doi.org/)
Online 19 May 2008

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Theodore A. Slotkin[1,2], Bethany E. Bodwell[1], Ian T. Ryde[1], Edward D. Levin[1,2] and Frederic J. Seidler[1]

[1]Department of Pharmacology & Cancer Biology
Duke University Medical Center
Durham, North Carolina USA

[2]Department of Psychiatry & Behavioral Sciences
Duke University Medical Center
Durham, North Carolina USA

Correspondence: Dr. T.A. Slotkin
Box 3813 DUMC
Duke Univ. Med. Ctr.
Durham, NC 27710
Tel 919 681 8015
Fax 919 684 8197
t.slotkin@duke.edu
Express mail:
Room C162 LSRC Bldg., Research Drive
Duke University Medical Center
Durham, NC 27710

Running title: Parathion Developmental Neurotoxicity

Acknowledgments/disclaimers: Research was supported by NIH ES10356. The authors have no competing financial interests. Theodore Slotkin and Frederic Seidler have provided expert witness testimony on behalf of government agencies, corporations and/or individuals.

Key words: Acetylcholine
Brain development
Organophosphate insecticides
Parathion

Abbreviations: ACh, acetylcholine
ANOVA, analysis of variance
ChAT, choline acetyltransferase
HC3, hemicholinium-3
nAChR, nicotinic acetylcholine receptor
OP, organophosphate
PN, postnatal day

Descriptors: Neurodevelopment
Developmental Biology

Outline of Section Headers

Abstract

Introduction

Materials and Methods
- Animal treatments
- Assays
- Data analysis
- Materials

Results

Discussion

References

Figure Legends

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ABSTRACT

Background: Organophosphates elicit developmental neurotoxicity through multiple mechanisms besides their shared property as cholinesterase inhibitors. Accordingly, these agents may differ in their effects on specific brain circuits. Objectives: We gave parathion to neonatal rats (postnatal days PN1-4), at daily doses of 0.1 or 0.2 mg/kg, spanning the threshold for barely-detectable cholinesterase inhibition and systemic effects. Methods: We assessed neurochemical indices related to the function of acetylcholine (ACh) synapses (choline acetyltransferase, presynaptic high-affinity choline transporter, nicotinic cholinergic receptors) in brain regions comprising all the major ACh projections, with determinations carried out from adolescence to adulthood (PN30, PN60, PN100). Results: Parathion exposure elicited lasting alterations in ACh markers in the frontal/parietal cortex, temporal/occipital cortex, midbrain, hippocampus and striatum. In cerebrocortical areas, midbrain and hippocampus, effects in males were generally greater than in females, whereas in the striatum, females were targeted preferentially. Superimposed on this general pattern, the cerebrocortical effects showed a nonmonotonic dose-response relationship, with regression of the defects at the higher parathion dose; this relationship has been seen also after comparable treatments with chlorpyrifos and diazinon, and likely represents the involvement of cholinesterase-related actions that mask or offset the effects of lower doses. Conclusions: Neonatal exposure to parathion, at doses straddling the threshold for cholinesterase inhibition, compromises indices of ACh synaptic function in adolescence and adulthood. Differences between the effects of parathion as compared to chlorpyrifos or diazinon, and the nonmonotonic dose-effect relationships, reinforce the conclusion that various organophosphates diverge in their effects on neurodevelopment, unrelated to their anticholinesterase actions.